

IN THE SPECIFICATION

Please replace the third paragraph on page 5 with the following paragraph: “Figure 3 shows electropherograms showing the sequence surrounding the mutations in the APECED gene. (A) Mutation analysis of a Swiss APECED family. The parents are heterozygous for the allele (normal “C” and abnormal “T”). The affected boy and girl show the “C” to “T” transition resulting in the “Arg” to “Stop” nonsense mutation at amino acid position 25 (B) Mutation analysis of two Finnish APECED patients. The patient MP is homozygous for the mutant allele (left), NP is heterozygous for the allele (right). (C) The patient NP shows the “A” to “G” transversion resulting in the “Lys” to Glu” missense mutation at amino acid position ~~42~~ 83.”

Please replace the second full paragraph on page 8 with the following paragraph: “The APECED gene is approximately 13-kb in length and contains 15 exons, including the exon 1' specific to AIR-2 and AIR-3. It is transcribed in the directed of centromere to telomere (Figs a, 2A). Based on this information, PCT primers were designed to amplify each exon from the genomic DNA and a mutation analysis of Swiss and Finnish APECED families was performed. Sequence comparison identified two mutations in the APECED gene of the patients (Fig. 3). The first mutation changes an Arg codon (CGA) to a stop codon (TGA) at amino acid position 257 in exon 6. This mutation was designated as R257stop mutation. The second mutation is a missense mutation that derived from the maternal chromosome in one Finnish patient (NP): a Lys codon (AAG) changes to a Glu codon (GAG) at amino acid ~~42~~ 83” in exon 2. This mutation is designated as ~~K42E~~ K83E mutation (Figs 2A, 3C).”

Please replace the third full paragraph on page 8 with the following paragraph, “ The R257 stop mutation destroys a Taql restriction enzyme site and the ~~K42E~~ K83E mutation introduces a novel Taql site. Thus these two mutations can be easily demonstrated in one or both alleles by Taql digestion or by digestion using another enzyme cleaving at the recognition site 5'-TCGA-3'(Fig. 4).”

Please replace the seventh paragraph of page 12 with the following paragraph, “ In the mutation analysis by sequencing, two Swiss and three Finnish (HP1, HP2 and MP) patients with APECED were homozygous for R257stop allele, whereas one Finnish patient (NP) was

heterozygous for this mutation (Fig. 3A, B). The R257stop mutation of NP was derived from the paternal chromosome. The second mutation, ~~K42E~~ K83E mutation, was found in one Finnish patient (NP): a Lys codon (AAG) changes to a Glu codon (GAG) at amino acid position ~~42~~ 83".

Please replace the second full paragraph on page 13, with the following: "For exon 2, the fragment containing the mutation site ~~K42E~~ K83E was amplified with primers GR1/2F and GR1/2R with the following conditions: 95°C for 3 min., 35 cycles of 94°C for 30 sec, 62°C for 30 sec and 72°C for 1 min. The 1x reaction mix used contained 50 mM KCl, 10 mM Tris-HCl, pH 8.3, 1.5 mM MgCl₂, 0.001% (w/v) gelatin, 0.2 mM each of dNTPs, 0.25 U of Dynazyme (Finnzymes, Finland), and 0.5 mM of each of the exon-specific primers. The normal allele produces a 312 bp fragment whereas the mutated allele gives a 133 bp and a 179 bp fragment. Primer sequences from GR1/2F and GR1/2R are 5'-TGGAGATGGGCAGGCCGCAGGGTG (sequence id. no. 21) and 5'-CAGTCCAGCTGGGCTGAGCAGGTC (sequence id. no. 22), respectively."

Please replace the fourth paragraph on page 13 with the following paragraph: "The screening of 50 Finnish and 50 Swiss healthy individuals did not reveal R257 stop or ~~K42E~~ K83E mutations by TaqI digestion. Similarly, PCR analysis of 20 unaffected Japanese was performed and no mutations were found in any of these positions. These results demonstrate that the APECED gene is responsible for the pathogenesis of APECED."